UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/897,427	07/03/2001	Jon Elliot Adler	P 0282558 2001-028A	8334

7590 09/30/2003

CROWELL AND MORING, LLP
INTEELCTUAL PROPERTY GROUP
P.O. BOX 14300
WASHINGTON, DC 20044-4300

EXAMINER	
LANDSMAN, ROBERT S	

ART UNIT	PAPER NUMBER
1647	20

DATE MAILED: 09/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/897,427	Applicant(s) ADLER ET AL.	
	Examiner Robert Landsman	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *100-148* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *100-148* is/are rejected.

7)☒ Claim(s) *100-148* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *18* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

1. Formal Matters

A. Amendment B, filed 7/25/03, has been entered into the record.

B. The Information Disclosure Statement, filed 7/25/03, has been entered into the record.

C. Amendment A, filed 5/15/03, has been entered into the record.

D. Claims 1-99 were pending in the application. In Amendment A, Applicants cancelled claims 1-99 and added new claims 100-146. In Amendment B, Applicants replaced new claims 100-146 with correctly numbered claims 100-148. Therefore, claims 100-148 are pending and are the subject of this Office Action.

E. All Statutes under 35 USC not found in this Office Action can be found, cited in full, in a previous Office Action.

F. While not the basis for a rejection or objection, the syntax of claim 101 could be improved by adding the phrase "hetero-oligomeric" after the phrase "T1R2/T1R3."

G. While not the basis for a rejection or objection, the syntax of claims 106 and 107 could be improved by capitalizing the letter "L" in "Hela."

H. While not the basis for a rejection or objection, the syntax of claims 143-146 could be improved by adding the word "sweet" between "putative" and "taste."

I. While not the basis of a rejection or objection, the syntax of claims 147 and 148 can be improved by placing commas around both recitations of the word "respectively."

2. Oath/Declaration

A. The objection to the Oath has been withdrawn in view of Applicants amendment to the first line of the specification which recites that the present application claims benefit of U.S. Provisional Applications 60/284,547 and 60/300,434. Since the information in the first line of the specification is what is relied upon, Applicants do not need to submit a new Oath to amend the incorrect priority claim to 60/880,606.

3. Title

A. The objection to the title has been withdrawn in view of Applicants' amendment to recite that the present invention is drawn to methods of using the taste receptors.

4. Specification

A. The objection to the specification has been withdrawn in view of Applicants amendment to the first line of the specification which recites that the present application claims benefit of U.S. Provisional Applications 60/284,547 and 60/300,434 and that "280606" was Applicants' own reference number. This information will be corrected on the Bibliographic Data Sheet prior to issuance upon the finding of any allowable subject matter, or Applicants may submit a request for a Corrected Filing Receipt.

B. The objection to the specification regarding the paragraph on page 69, lines 12-22 has been withdrawn in view of Applicants' amendments to the underlining of "herein" as well as to amending "Ga15" to recite "Gα15."

C. The objection to the specification regarding referencing provisional U.S. Application 60/243,770 has been withdrawn since, even though the specification still references provisional U.S. Application 60/243,770, this application and the present application have a common assignee. It is brought to Applicants' attention, however, that if the present application issues as a patent, 60/243,770 will become public knowledge.

5. Claim Objections

A. The objections to claims 1 and 2 as recited on page 3 of the Office Action dated 12/23/02, regarding the words "as" and "measured by assayed," respectively, have been withdrawn in view of the cancellation of these claims and the fact that the new claims do not raise these issues.

B. Claims 100-148 are objected to since claim 100 recites "modulates, inhibits or activates" and claim 101 recites "modulates, enhances, or inhibits." This appears to be redundant since inhibition and activation/enhancing are forms of modulation. Claims 102-148 are also objected to since they depend from claims 100 or 101.

C. Claims 108-111 are objected to since claims 108 and 109 recite that the G protein couples the T1R polypeptides. It is believed that the phrase should recite "couples to" since, as written, it appears that the G protein is physically linking the two receptors of the heterodimer. Claim 114 is also objected to since it depends from claim 111. However, as seen in paragraph E of this section, it is probable that claim 114 was not intended to depend from claim 111.

D. Claims 113, 117, 119, 123, 127, 129, 131 and 133 are objected to since, even though it is clear that the recitation of "activity" in these claims is in reference to the "activation" recited in claim 101, all of the claims should be consistent with each other by being amended to recite either "activity" or "activation." No rejection under 35 USC 112, second paragraph, is being made regarding a lack of antecedent basis since the intention of the dependent claims is clear and is simply a matter of syntax.

E. Claims 114 and 115 are objected to since it appears that Applicants intended these claims to depend from claims 112 and 113, respectively, instead of from claims 111 and 112, respectively. If the dependency is, in fact, correct, then a rejection under 35 USC 112, second paragraph, will be made since claim 114 would then lack antecedent basis since claim 111 does not recite "Ca^{2+} levels." However, this numbering simply appears to be a typographical error.

F. Claims 120 and 121 are objected to since it appears that Applicants intended these claims to depend from claims 118 and 119, respectively, instead of from claims 117 and 118, respectively. If the dependency is, in fact, correct, then a rejection under 35 USC 112, second paragraph, will be made since claim 120 would then lack antecedent basis since claim 117 does not recite "second messenger." However, this numbering simply appears to be a typographical error. Claim 124 is objected to since it depends from claim 121.

G. Claims 124 and 125 are objected to since it appears that Applicants intended these claims to depend from claims 122 and 123, respectively, instead of from claims 121 and 122, respectively. If the dependency is, in fact, correct, then a rejection under 35 USC 112, second paragraph, will be made since claim 124 would then lack antecedent basis since claim 121 does not recite "cyclic nucleotide." However, this numbering simply appears to be a typographical error.

H. Claims 128 and 129 are objected to since it appears that Applicants intended these claims to depend from claims 112 and 113, respectively, instead of from claims 111 and 112, respectively.

I. Claims 134 and 135 are objected to since the syntax could be improved by replacing the word "is" with "uses" since a high-throughput screening assay is not a method, but a system used in a method.

J. Claims 136 and 137 are objected to since it appears that Applicants intended these claims to depend from claims 134 and 135, respectively, instead of from claims 133 and 134, respectively.

K. Claim 142 is objected to since the syntax could be improved by removing the word "activity" and replacing it with the phrase "consisting of:" or "comprising:."

L. Claim 143 is objected to since the claim should recite "activates" instead of "enhances the activity of" since the term "activates" and not "enhances" is recited in claim 100, from which claim 143 depends. No rejection under 35 USC 112, second paragraph, is being made regarding a lack of antecedent basis since the terms "activates" and "enhances" are similar with regards to their definition in the art and is, therefore, simply a matter of syntax.

M. Claims 147 ad 148 are objected to since the syntax could be improved by replacing the phrase "contained in" with "of."

6. Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

A. Claims 100-115 and 118-148 are provisionally rejected under the judicially created doctrine of double patenting over claims 21, 24-26, 44, 51, 53-60 and 72 of copending Application No. 10/179,373. All claims of the co-pending application ultimately depend from claim 21. Application 10/179,373 was not available to the Examiner at the Office Action dated 12/23/02 was written. However, Applicants were informed that a provisional double patenting rejection may be made in a subsequent Office Action. The rejection is as follows:

Claims 100 and 101 of the present invention recite a method of screening for compounds that modulate, inhibit, activate, or enhance sweet taste signaling of a T1R2/T1R3-expressing cell in the presence or absence of known sweet compounds. Claim 44 of the co-pending application recites a method

for identifying compounds which modulate, activate or inhibit sweet taste perception by using T1R2/T1R3 receptors. Though the method of claim 44 is not as complete as those recited in claims 100 and 101 of the present invention, it would have been obvious to one of ordinary skill in the art at the time of the present invention to have performed the method steps of claims 100 and 101 of the present application by using the methods steps of the co-pending application since the methods of the co-pending application encompass those of the present invention. The artisan would have been motivated to have used the methods of the co-pending application since it was well-known in the art at the time that screening methods normally require contacting a cell expressing the receptors of interest with a test compound either in the absence or presence of a known compound in order to determine (i.e. assay) the effects of said compound, therefore, rendering claims 100 and 101 of the present invention obvious. There would have been a reasonable expectation of success at the time of the present invention in practicing the methods of the present invention since methods for screening ligands were widely used and highly successful in the art at the time of the present invention. All claims in the co-pending application ultimately depend from claim 21 and, therefore, the obviousness, motivation and expectation of success in performing the remaining methods discussed in this rejection would at least encompass these reasons. Therefore, only the specific differences between the claims of the present invention and those of the co-pending application are discussed below.

Claims 102-107 are provisionally rejected over claim 51 the co-pending application. Claims 102-107 recite that the claimed methods are performed in mammalian eukaryotic cells, including CHO, HeLa or HEK-293 cells. HEK-293, COS and CHO cells, as recited in claim 51 of the co-pending application are, in fact, mammalian eukaryotic cells. In fact, claim 51 recites cell lines as claimed in claims 106 and 107. Claims 108-111 are provisionally rejected over claims 58-60 of the co-pending application. Claims 108-111 recite the use of cells expressing G-proteins which couple (to) T1R polypeptides. This includes the use of Gα15 and Gα16, which are promiscuous G proteins. These limitations are recited in the co-pending application. Though claims 58-60 do not recite that the G proteins couple to T1R polypeptides, it would be an inherent property of Gα15 and Gα16, sine these are promiscuous G proteins which, by definition, couple to nearly all G protein-coupled receptors. In fact, Example 3 of the co-pending application demonstrate that the T1R2/T1R3 heterodimer is functional in the presence of Gα15. This is also disclosed in the present specification in the sentence bridging pages 9-10 as well as in Example 6.

Claims 112-115 and 126-129 of the present invention are provisionally rejected over claims 55 and 57 of the co-pending application. Claims 112-113 recite measuring intracellular calcium levels, which meets the limitation of claim 55 since Ca^{2+} is a second messenger which is known to couple to T1R

polypeptides. Claims 126-129 recite measuring this calcium change by a change in fluorescence and by using fluorimetric imaging, which include the calcium-sensitive dyes FURA-2, FURA-3 and Fluo-4; therefore, meeting the limitation of claim 57 of the co-pending application. Claims 114-115 recite using a voltage fluorescence indicator, which is met by claim 57 since voltage-sensitive dyes are one form of a voltage fluorescence indicator. Regardless, it would have been obvious to one of ordinary skill in the art at the time of the present invention to have used any voltage or fluorescence indicator in the present invention in place of the voltage- or calcium-sensitive dye taught in the copending application since the goal of all of these forms of measurement accomplish the same goal – to measure a change in voltage or calcium levels upon the addition of a test compound. Therefore, the artisan would have been motivated to use any calcium or voltage fluorescence indicator, including dyes, to measure voltage or calcium since the use of dyes and other fluorescence techniques were well-known and highly successful in the art at the time of the present invention.

Claims 118-119 and 130-131 of the present invention are provisionally rejected over claim 55 of the co-pending application since both applications recite the use of second messengers. GTPγS is a second messenger. Claims 120-125 of the present invention are provisionally rejected over claim 56 of the co-pending application since the claims in both applications recite the use of IP_3 and cAMP (a cyclic nucleotide). Claims 132-133 of the present invention are provisionally rejected over claims 53 and 54 of the co-pending application since the present application recites monitoring a ligand in the kinase/arrestin pathway. Claim 53 recites measuring receptor phosphorylation, which, by definition, is produced by kinases, as recited in claims 132 and 133. Claim 54 recites measuring arrestin translocation, which is an arrestin pathway associated with receptor phosphorylation, as recited in claims 132 and 133. Both of these mechanisms are well-known in the art to be involved in receptor desensitization. Therefore, since T1R polypeptide were known at the time of the present invention to be involved in phosphorylation (i.e. kinase activity) and arrestin translocation, as recited in the co-pending application, it would have been obvious to the artisan to have measured for ligands which affect this kinase/arrestin pathway. Though the exact ligand to be measured raises issues under 35 USC 112, first paragraph, regarding enablement and written description as seen in the below rejections, the idea of measuring affects on the kinase/arrestin pathway would, regardless, have been obvious, again, due to the well-known affect of the arrestin/kinase pathway on GPCR receptor desensitization.

Claims 134-137 of the present invention are provisionally rejected over claim 72 of the co-pending application since both applications recite the use of high-throughput screening assays. Though the co-pending application does not recite the use of a combinatorial chemical library, it would have been

obvious for the artisan to have used a combinatorial library since these large libraries would be well-suited for a high-throughput screening assay. Therefore, the artisan would have been motivated to test any large library, including combinatorial libraries, in a high-throughput assay in order to most efficiently screen the largest number of compounds in the shortest amount of time. Claims 138-141 of the present invention are provisionally rejected over claims 24-26 of the co-pending application since both applications recite the use of T1R2 and T1R3 receptors from different species. Claim 26 of the co-pending application recites that the T1R2 and T1R3 proteins are derived from mammals, which meets the limitation of claims 138-141 since humans, rats and mice are mammals.

Claim 142 of the present invention is provisionally rejected over claim 44 of the co-pending application. Though the co-pending application does not specifically recite the use of a known sweet ligand, it would have been obvious for one of ordinary skill in the art to have used a known sweet ligand, including, for example, the sugar, sucrose, in the co-pending application since it is common in the art that when attempting to identify putative ligands for binding to and/or activation of a receptor, a known ligand should be used in a competition assay as a reference. Claim 21 of the co-pending application makes it clear that the receptor of that invention is a sweet receptor. Therefore, one would have been motivated to use a known sweet ligand such as sucrose or fructose in that invention in order to identify competing ligands which activate or modulate the sweet taste receptor. There would have been a reasonable expectation of success in performing this method since these methods are the standard assay procedures for putative ligand identification in the art. Finally, claims 143-146 are also rejected over claim 44 of the co-pending application since all of these claims involve identifying compounds which enhance or inhibit the activity or activation of the receptor.

7. Claim Rejections - 35 USC § 112, first paragraph – scope of enablement

A. The rejection of claims 3, 4, 9 and 10 under 35 USC 112, first paragraph, has been withdrawn in view of the cancellation of these claims and that the newly submitted claims do not raise the issue of "at least one additional nucleic acid construct." Regarding new claims 108 and 109, the Examiner agrees that due to the limited number of G proteins known in the art, the selection of an appropriate G protein for use in the present invention would not rise to the level of undue experimentation.

B. Claims 132 and 133 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of screening compounds using assays which measure changes in Ca^{2+}, IP_3, cGMP, voltage, GTPγS and cAMP, does not reasonably provide enablement for these methods using any ligand in the kinase/arrestin pathway. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

First, the breadth of the claims is excessive with regard to Applicants claiming detecting changes in receptor activity by monitoring any and all ligands in the kinase/arrestin pathway. Applicants have provided no guidance or working examples of which ligands in this pathway could be measured, nor what these results would conclude. Though it is known in the art that the kinase/arrestin pathway *in general* is involved in the desensitization of GPCRs, Applicants provide no discussion in the specification as to what ligands are involved in this pathway. Without this teaching, Applicants have not enabled the methods of claims 132 and 133. Furthermore, due to the lack of guidance and working examples as to what ligands exist in the kinase/arrestin pathway and what the information gathered by monitoring these ligands would conclude, it would be unpredictable to the artisan what ligands to monitor and what information could be gathered as a result.

Therefore, in summary, the breadth of the claims is excessive with regard to Applicants claiming a method of screening compounds by monitoring any and all ligands in the kinase/arrestin pathway. Applicants have provided no guidance or working examples of any ligands in this pathway, nor what the results of measuring these ligands would be, or, more specifically, what could be concluded regarding the compounds used in the screening assays of the claimed methods. Due to this excessive breadth and lack of guidance and working examples, it would not be predictable to the artisan what ligands in the kinase/arrestin pathway could be measured or what pertinent information regarding the screened compounds could be gathered as a result. For these reasons, the Examiner holds that undue experimentation would be required to practice the invention as claimed.

C. Claims 147 and 148 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of screening compounds using polypeptides encoded by SEQ ID NO:3 and 5, as well as for "T1R2/T1R3 heterodimers," does not reasonably provide enablement for these methods using any DNA which hybridizes to SEQ ID NO:3 or 5 wherein the taste receptors respond to sweet stimuli. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

First, the breadth of the claims is excessive with regard to Applicants claiming the screening methods of claims 147 and 148 by using any and all taste receptors encoded by polynucleotides which hybridize to SEQ ID NO:3 and 5 and which respond to sweet stimuli. Even if Applicants recited exact hybridization conditions, as discussed below in the rejection of these claims under 35 USC 112, second paragraph, the breadth would remain excessive. Applicants have only provided guidance and working examples of T1R2 and T1R3 polypeptides encoded by SEQ ID NO:3 and 5 (SEQ ID NO:4 and 6, respectively). However, given the teachings cited on page 7, lines 16-20 and page 14, lines 12-15 of the specification, which demonstrate that the art recognizes the family of T1R receptors, and that this small family of receptors can be identified based on morphology, it is clear that the art recognizes T1R2 and T1R3 receptors and, therefore, Applicants are enabled for screening for T1R2/T1R3 heterodimers. However, Applicants are not enabled for the claimed methods by identifying or using any receptor which responds to sweet taste stimuli other than the known T1R2 and T1R3 receptors. Applicants have not taught which residues are critical for T1R2/T1R3 polypeptide function and, therefore, which residues would need to be maintained in order to maintain the function of the claimed polypeptides for receptors other than T1R2 and T1R3. Therefore, it would not have been predictable for one of ordinary skill in the art at the time of the present invention how to make any other "sweet taste receptors" other than T1R2 and T1R3, including those encoded by SEQ ID NO:3 and 5.

Therefore, in summary, the breadth of the claims is excessive with regard to Applicants claiming methods of screening ligands by using any and all proteins which respond to sweet stimuli other than T1R2 and T1R3, which include those encoded by SEQ ID NO:3 and 5. Applicants have provided no guidance or working examples of any polypeptides which can form a heterodimer which responds to sweet taste stimuli other than T1R2 and T1R3 polypeptides, including those encoded by SEQ ID NO:3 and 5, nor have Applicants taught which amino acid residues are critical to retain protein function in order to produce other functional "receptors which respond to sweet taste stimuli." Therefore, it would not be predictable to the artisan how to make a functional protein to be used in the claimed methods other than T1R2 and T1R3 polypeptide, including those encoded by SEQ ID NO:3 and 5. For these reasons, the

Examiner has concluded that undue experimentation would be required to practice the invention as claimed.

8. Claim Rejections - 35 USC § 112, first paragraph – written description

A. Claims 132 and 133 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These are genus claims. The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus of "a ligand in the arrestin/kinase pathway." Thus the scope of the claims includes numerous variants, and the genus is highly variant because a significant number of structural and functional differences between genus members is permitted. The specification and claims do not provide any guidance as to what ligands occur in this pathway. Therefore features that could distinguish compounds in the genus from others not involved in the kinase/arrestin pathway are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, "a ligand in the arrestin/kinase pathway" alone is insufficient to describe the genus. One of skill in the art would reasonable conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus at the time the invention was made.

B. Claims 147 and 148 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These are genus claims. Methods of screening compounds using receptors encoded by DNA which hybridizes to SEQ ID NO:3 and 5 would use proteins with one or more amino acid substitutions, deletions, insertions and/or additions to the proteins encoded for by SEQ ID NO:3 and 5. Applicants have only provided adequate written description for the use of T1R2 and T1R3 receptors, including those of SEQ ID NO:4 and 6 of the present invention. No other species of "receptors which respond to sweet taste stimuli" are described, or structurally contemplated, within the instant specification. Therefore, one

skilled in the art cannot reasonably visualize or predict critical amino acid residues which would structurally characterize the genus of amino acids comprising the genus of "sweet taste receptors" claimed, because it is unknown and not described what structurally constitutes any different sweet taste receptors, or sweet taste receptors from any different species, which are further not described, other than T1R2 and T1R3, which includes those encoded by SEQ ID NO:3 and 5. The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. No common structural attributes identify the members of the genus and structural features that could distinguish compounds in the genus from others in the nucleic acid or protein class, as well as guidance as to what changes should be made, are missing from the disclosure. Thus the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, "receptors which respond to sweet taste stimuli," including SEQ ID NO:4 and 6, or proteins which are encoded by molecules which hybridize to SEQ ID NO:3 and 5, alone, are insufficient to describe the genus.

Therefore, one of skill in the art would reasonable conclude that the disclosure fails to provide a representative number of species to describe the genus; thereby not meeting the written description requirement under 35 USC 112, first paragraph. Thus, Applicant was not in possession of the claimed genus at the time the invention was made.

9. Claim Rejections - 35 USC § 112, second paragraph

A. The rejection of claims 1-11 under 35 USC 112, second paragraph, regarding "activity" has been withdrawn in view of the cancellation of these claims and Applicants' arguments that the specification discloses numerous assays for measuring receptor "activity" and that the claims specifically identify such assays (i.e. activities). Therefore, this issue will not be raised for the newly added claims.

B. The rejection of claims 1-11 under 35 USC 112, second paragraph, regarding the recitation of an end step has been withdrawn in view of Applicants' cancellation of these claims and in view of Applicants' arguments that new claims 100 and 101, as well as pages 50-53 of the specification, make it clear (i.e. provide an "end-step") that a detectable change in receptor activity correlates to the putative

modulator being identified as a sweet taste modulator, inhibitor, or enhancer. The Examiner agrees that, especially given the teachings on pages 50-53 of the specification, in combination with the knowledge in the art, that artisan would readily known when a compound activates, inhibits, enhances (i.e. modulates) sweet taste signaling.

C. The rejection of claim 6 under 35 USC 112, second paragraph, regarding the it being unclear if the two receptors in part (ii) are the same as in part (i) has been withdrawn in view of the cancellation of claim 6 and that no new claims raise this issue.

D. The rejection of claim 7 under 35 USC 112, second paragraph, regarding "modulatory compounds" and what it is that these compounds activate has been withdrawn in view of the cancellation of claim 7. None of the newly added claims raise this issue.

E. Claims 132 and 133 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: an end-step explaining what the data obtained from the ligand being monitored conclude. Applicants have not identified a specific ligand to be monitored in this assay. Therefore, it would be unclear as to what endpoints to monitor, or what data this information will provide.

F. Claim 142 recites the limitation "known sweet ligand" into claim 101. There is insufficient antecedent basis for this limitation in the claim. Claim 101 recites "known sweet *compound*."

G. Claims 147 and 148 are vague and indefinite since the claims recite "moderately stringent conditions." It is not known what these hybridization conditions are. Therefore, it is required that Applicants amend the claims to recite the exact hybridization conditions without using indefinite phrases such as "*for example,*" which can be seen in the sentence bridging pages 25 and 26 of the specification, **and without adding new matter**.

10. Claim Rejections - 35 USC § 103

A. The rejection of claims 1-11 under 35 USC 103 as being unpatentable over Zuker et al. (U.S. Patent No. 6,383,778) in view of Montmayeur et al. (Nat. Neurosci.) has been withdrawn in view of Applicants' arguments. Applicants argue that the present invention involves the discovery that cells which co-express T1R2 and T1R3, as opposed to expressing only one or the other receptor, produce a functional sweet taste receptor. Applicants also argue that Zuker et al. do not teach T1R3 receptors, which is required in all of the present claims, nor does the patent teach that the co-expression of T1R2 and T1R3 would produce a functional sweet taste receptor. Applicants further argue that while Montmayeur et al. teach that T1R2 and T1R3 may be expressed in the same cell and suggest that these receptors may form heterodimers, neither Montmayeur et al. nor Zuker et al. teach the formation of this heterodimer. Even, *arguendo*, these receptors were shown to form heterodimers, neither Zuker et al. nor Montmayeur et al. provide any motivation to specifically test this receptor combination (i.e. heterodimer) in an assay to identify sweet taste compounds. In fact, as argued by Applicants, Montmayeur et al. even teach away from T1R3 being involved in sweet taste signaling by stating in the first full paragraph of page 496 that it is possible that "T1R3 is not a sweet taste receptor gene."

11. Conclusion

A. No claim is allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
September 29, 2003

ROBERT LANDSMAN
PATENT EXAMINER